WEST

End of Result Set

☐ Generate Collection

L2: Entry 2 of 2 File: USPT May 16, 2000

DOCUMENT-IDENTIFIER: US 6064754 A
TITLE: Computer-assisted methods and apparatus for identification and characterization of biomolecules in a biological sample

DEPR:
The amino acid sequences of one or more peptides derived from a removed protein can now be determined, for instance by a suitable mass spectrometry technique, such as matrix-assisted laser desorption/ionization combined with time-of-flight mass analysis (MALDI-TOF MS) or electrospray ionization mass spectrometry (ESI MS). See Jensen et al., 1977, Protein Analysis By Mass Spectrometry, In Creighton (ed.), Protein Structure, A Practical Approach (Oxford University Press), Oxford, pp. 29-57; Patterson & Aebersold, 1995, Electrophoresis 16: 1791-1814; Figeys et al., 1996, Analyt. Chem. 68: 1822-1828 (each of which is incorporated herein by reference in its entirety). Preferably, a separation technique such as HPLC or capillary electrophoresis is directly or indirectly coupled to the mass spectrometer. See Ducret et al., 1996, Electrophoresis 17: 866-876; Gevaert et al., 1996, Electrophoresis 17: 918-924; Clauser et al., 1995, Proc. Natl. Acad. Sci. USA 92: 5072-5076 (each of which is incorporated herein by reference in its entirety). Especially preferred is the de novo sequencing technique described in U.S. patent application Ser. No. 08/877,605, which is incorporated herein by reference in its entirety. In de novo sequencing, the molecular mass of the peptide is accurately determined by any suitable technique, preferably with a mass spectrometer. A computer is used to determine all possible combinations of amino acids that can sum to the measured mass of the peptide, having regard to water lost in forming peptide bonds, protonation, other factors that alter the measured mass of amino acids, and experimental considerations that constrain the allowed combinations of amino acids. The computer then constructs an allowed library of all linear permutations of amino acids in the permitted combinations. Theoretical fragmentation spectra are then calculated for each member of the allowed library of permutations and are compared with an experimental fragmentation spectrum obtainable by mass spectrometry for the unknown peptide to determine the amino acid sequence of the unknown peptide. Most preferably, tandem mass spectrometry is used to determine the amino acid sequence of the unknown peptide.

FILE 'HOME' ENTERED AT 06:50:06 ON 15 AUG 2001)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 06:50:22 ON 15 AUG 2001

L1	627	S	POST (W)SOURCE(W)DECAY
L2	82	S	L1 (P)(MALDI(W)TOF(W)MS)
L3	0	S	L2 (P)NUCLEIC
L4	8	S	L2 (P)COMPUTER?
L5	1863	S	(MALDI(W)TOF(W)MS)
L6	24	S	L5 (P)NUCLEIC
L7	0	S	L6 (P)PEAK
L8	0	S	L6 (P)REFERENCE
L9	5	S	L6(P)CLEAV?

End of Result Set

☐ Generate Collection

L3: Entry 3 of 3 File: USPT Sep 15, 1998

DOCUMENT-IDENTIFIER: US 5808300 A
TITLE: Method and apparatus for imaging biological samples with MALDI MS

BSPR:
Capillary electrophoresis (CE) and matrix-assisted laser desorption ionization mass spectrometry (MALDI MS) are combined in an off-line arrangement to provide separation and mass analysis of peptide and protein mixtures in the attomole range. A membrane target, precoated with MALDI matrix was used for the continuous deposition of effluent exiting from a CE device. A sample track was produced by linear movement of the target during the electrophoretic separation and this track was subsequently analyzed by MALDI MS. The technique is effective for peptides and proteins, having limits of detection (S/N>3) of about 50 attomoles for neurotensin (1,673 daltons) and 250 attomoles for cytochrome c (12,361 daltons) and apomyoglobin (16,951 daltons). The electrophoretic separation achieved from the membrane target, as measured by theoretical plate numbers from the mass spectrometric data, can be as high as 80-90% of that achieved by on-line UV detection under optimal conditions, although band broadening occurs and can decrease separation efficiency. Non-volatile buffers such as 10-50 mM phosphate can also be used in the electrophoresis process and directly deposited on the membrane. The use of post-source decay techniques is shown for peptides in the CE sample track in order to obtain sequence verification. The effectiveness of this method of integration of CE and MALDI MS is demonstrated with both peptide and protein mixtures and with the analysis of a tryptic digest of a protein.